European Cystic Fibrosis Society

Journal of Cystic Fibrosis
The Official Journal of the European Cystic Fibrosis Society

Cystic Fibrosis Research News

Title:

Laboratory reporting on the clinical spectrum of CFTR p.Arg117His: still room for improvement

Authors:

Nele Laudus[1], Marie-Pierre Audrézet[2], Emmanuelle Girodon[3], Michael A Morris[4], Dragica Radojkovic[5], Caroline Raynal[6], Manuela Seia[7], Alexandra Štambergová[8], Heike Torkler[9], Raina Yamamoto[9], Elisabeth MC Dequeker[1, 10].

Affiliations:

1 Biomedical Quality Assurance Research Unit, Department of Public Health and Primary Care, University of Leuven, Leuven, Belgium.
2 Laboratoire de Génétique Moléculaire, CHU Brest, Brest, France.
3 Laboratoire de Génétique et Biologie Moléculaires, AP-HP.Centre-Université de Paris, Hôpital Cochin, Paris, France.
4 SYNLAB Genetics, Lausanne, Switzerland.
5 Laboratory for Molecular Biology, Institute of Molecular Genetics and Genetic Engineering, University of Belgrade, Belgrade, Serbia.
6 Laboratoire de Génétique Moléculaire, CHU de Montpellier, Montpellier, France.
7 Laboratorio di Genetica Medica - Settore di Genetica Molecolare, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy.
8 Department of Biology and Medical Genetics, 2nd Faculty of Medicine, Charles University in Prague and Motol University Hospital, Prague, Czech Republic.
9 MVZ Dr. Eberhard & Partner Dortmund, Dortmund, Germany. 10 Department of Medical Diagnostics, University Hospitals Leuven, Leuven, Belgium.

What was your research question?

Most individuals carrying CFTR mutation p.Arg117His on a 7T-background remain healthy throughout life or develop so-called CFTR-related disorders like male infertility and lung problems. Only in very few cases does clinically symptomatic cystic fibrosis occurs. We wanted to look at how accurately genetics laboratories report on this mutation to clinicians and to patients.

Why is this important?

Over 2000 mutations have already been identified in the CFTR gene. However, not all mutations cause cystic fibrosis. CFTR p.Arg117His is a relatively common mutation in Western

populations and it is known that people with this mutation can have really diverse levels of disease. Correct interpretation of clinical significance in laboratory reports has implications for patients' diagnosis, prognosis, therapeutic options and further follow-up, as well as for genetic counselling for patients and their relatives. External quality assessment schemes are a tool for laboratories to test themselves and evaluate how well they are doing compared with other laboratories.

What did you do?

Since more than twenty years, the CF Network has organized external quality assessment schemes for genetic laboratories. Laboratories receive DNA samples and fictional patient information and are asked to test for CFTR mutations and report on their results. Afterwards, laboratory reports are scored based on the presence of pre-defined, case-specific criteria which are considered important elements in reporting. Over the years, similar cases were introduced in the schemes. We investigated laboratory performance regarding the interpretation of p.Arg117His.

What did you find?

Overall, laboratories reported well on p.Arg117His. Nevertheless, some laboratories failed to clearly indicate that individuals carrying this mutation are highly unlikely to develop cystic fibrosis, in typical manifestation. Leading to potentially inappropriate prenatal and preimplantation genetic diagnostic testing subsequent births, as well as carrier testing in relatives, despite international recommendations. In addition, we found that laboratories that previously participated in our schemes performed better than laboratories that never participated before.

What does this mean and reasons for caution?

It is important that laboratories clearly and correctly report on this mutation so that unnecessary physical and emotional harm can be avoided. In addition, this study highlighted the educational role of external quality assessment schemes for laboratories.

What's next?

It will be interesting to find out if laboratory reporting on p.Arg117His will improve even more over time and to perform such evaluations over time for other mutations.

Original manuscript citation in PubMed

https://pubmed.ncbi.nlm.nih.gov/32505523/